REMARKS

Claims 35-45 are pending. A "clean" claim set to be introduced in place of the original claims is provided above. Support for amended claims 37 and 41 is found in the specification at page 24, lines 11-24. Support for amended claim 38 is found at page 18, lines 6-8; page 19, lines 5-7. Attached hereto is a version showing changes made for the Examiner's convenience. In addition, an appendix of the pending claims is attached for the Examiner's convenience.

Rejections based under 35 U.S.C § 101

Claims 35-45 are rejected under 35 U.S.C. § 101 as not being supported by a specific and substantial utility or a well established utility.

The Examiner states that the activity of the BLNK protein has not been defined and is largely speculative. The Examiner further states that the utility is a general utility and not a specific utility because the modulation of BCR regulation of calcium levels is not shown to be a factor in any disease or condition identifiable or treatable with a BLNK protein. Applicants respectfully disagree.

The Federal Circuit has stated, "[t]o violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result. MPEP § 2107.01 citing to" *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F. 2d 1555, 1571, 24 USPQ2d 1401, 1412 (Fed. Cir. 1992)(emphasis added). If an invention is only partially successful in achieving a useful result, a rejection of the claimed invention as a whole based on lack of utility is not appropriate. See *In re Brana*, 51 F. 3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995).

Rejections under 35 U.S.C. 101 have been rarely sustained by federal courts. Generally speaking, in these rare cases, the 35 U.S.C. 101 rejection was sustained either because the applicant failed to disclose any utility for the invention or asserted a utility that could only be true if it violated a scientific principle, such as the second law of thermodynamics, or a law of nature, or was wholly inconsistent with contemporary knowledge in the art. MPEP 2107.02 citing to, *In re Gazave*, 379 F. 2d 973, 978, 154 USPQ 92, 96 (CCPA 1967).

The claims of the present invention do not violate any scientific principle and Applicants have asserted a utility, namely that BLNK proteins interact with a variety of proteins in B cells. These interactions of BLNK proteins with such proteins as Grb2, PLC, nck adaptor protein and vav protooncogene is known by persons skilled in the art to be involved in downstream cell signaling pathways which among other events leads to cell proliferation and/or cell differentiation in B cells.

The fact that BLNK protein has a specific pattern of expression in B cells and substantially lower levels of expression, if any at all, in other tissue types would suggest to one skilled in the art that BLNK protein plays an important role in B cell development. See specification at page 19, lines 19-23. The signaling pathway through the B cell antigen receptor, of which BLNK protein plays a role has been shown to be important in understanding and finding treatments for immunodeficiency diseases, such as , but not limited to x-linked agammaglobulinemia in man. See *Desiderio et al. , The B cell antigen receptor in B-cell development, Curr Opin Immunol.* 1994 Apr; 6(2): 248-56. This would be considered by those skilled in the art to be a specific utility because now an important regulator of B-cell

development can be exploited in piecing together the complex interactions in B-cell development. See specification at page 1, lines 11-24.

In addition, another specific utility is screening for binding partners of BLNK protein's interaction with B cell proteins such as Grb2 which is involved in the cell signaling pathway through ras , following engagement of the BCR. This is another example of how BLNK is involved in modulating BCR signaling events which may provide a rational approach in the treatment of B-cell mediated tumors and also in autoimmune diseases in which aberrant B-cell activation may occur.

In addition, the fact that BNLK protein when overexpressed can elevate intracellular calcium levels independent of its interaction with phospholipase C is yet another example of a specific utility that can be exploited in understanding how increased intracellular calcium levels effect various stages of B cell development. See specification at page 19, lines 1-9.

BLNK proteins are specific to B cells and its effects on specific downstream signaling pathways involving RAS and PLCλ would be considered by those skilled in the art to be an important molecule that can exploited in gaining insight into B cell development and prove useful in therapeutic approaches involving B cell abnormalities. If an invention is only partially successful in achieving a useful result, a rejection of the claimed invention as a whole based on lack of utility is not appropriate. MPEP § 2107.01(II), citing to *In re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995).

In addition, the utility of BLNK proteins to modulate BCR mediated signaling events would be considered by those skilled in the art to be a public benefit and hence a substantial utility. Any reasonable use that an applicant has identified for the invention that can be viewed as

providing a public benefit should be sufficient, at least with regard to defining a "substantial" utility. See MPEP § 2107.02. See also *Nelson v. Bowley*, 206 U.S.P.Q. 881 (C.C.P.A. 1980), where the Court of Customs and Patent Appeals held that tests establishing pharmacological activity, such as stimulation of smooth muscle tissue from gerbil colons, and the modulation of blood pressure in rats, manifest a practical utility "even though they may not establish a specific therapeutic use." BNLK's ability to mediate BCR mediated signaling events manifests a practical utility even though it may not establish a specific therapeutic use. "Knowledge of the pharmological activity of any compound is obviously beneficial to the public. It is inherently faster and easier to combat illnesses and alleviate symptoms when the medical professional is armed with an arsenal of chemicals having known pharmological activities." *Nelson v. Bowley*, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980).

The ability of BLNK protein to modulate BCR mediated signaling events (specification at page 19, lines 1-17) is a specific and a substantial utility and therefore a rejection based on a lack of utility is improper in this instance. Applicants respectfully request the withdrawal of the rejection.

The declaration under 37 CFR 1.132 of inventor Chan

The Examiner states that there is no explanation or supporting evidence provided to establish a specific and substantial utility. Applicants respectfully disagree. The interaction of BLNK with Grb2, Phospholipase C and vav protooncogene and this interaction's ability to mediate BCR signaling events finds support in the specification at page 19, lines 1-17. One skilled in the art would realize the significance of BLNK in B cell development as modulation of

BCR mediated signaling events are known in the art to be important in cellular differentiation and development.

Rejection under 35 U.S.C. § 112, first paragraph: New matter

Claim 38 is rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully disagree.

Claim 38 describes a recombinant BLNK protein according to claim 37, which means that this BLNK protein which lacks at least one tyrosine phosphorylation site comprises (1) an amino acid sequence having at least about 95% identity to the amino acid sequence set forth in SEQ ID NO:1 and (2) wherein said BLNK protein binds to a protein selected from the group consisting of Grb2, PLCλ, vav and Nck (claim 37 which depends from claim 35). Therefore , one skilled in the art would be able to understand the BLNK protein of claim 38 would include only the proteins screened after mutagenesis procedures that still had 95% identity to the amino acid sequence set forth in SEQ ID No:1 and binds to a protein selected from the group consisting of Grb2, PLCλ, vav and Nck.

The nucleic acid sequence for BLNK-1(SEQ ID NO:1) has been provided to the PTO and one skilled in the art would be able to utilize known mutagenesis procedures to arrive at a BLNK protein lacking at least one tyrosine phosphorylation site having the defined characteristics of maintaining 95% homology to SEQ ID NO:1 and still being able to bind to any of the proteins selected from the group consisting of Grb2, PLCλ, vav and Nck. The BLNK protein of claim 38, which depends from claim 37, is properly defined to convey to one of

ordinary skill in the art that the applicants , at the time the application was filed, had possession of the claimed invention. Applicants, respectfully request the withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, first paragraph: Lack of written description

Claims 35-45 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The examiner states that the Applicant has not provided sufficient teaching or guidance to enable one skilled in the art to determine the specific sequences that are within the scope of the claims. Applicants respectfully disagree.

The Applicants have provided a schematic diagram depicting the structural formula of BLNK proteins (figure 7), in which three different structural regions , an N terminus, a central region and the C-terminus are defined structurally. The N-terminus of BLNK protein contains an acidic region (amino acids 51-109) and also tyrosine phosphorylation sites at Tyr 71, Tyr 83, Tyr 95, Tyr 177, and Tyr 187 (human BLNK numbering). The central region of BLNK proteins contain a proline rich region, amino acids 130-145. The C-terminus of BLNK proteins contains an SH2 domain, amino acids 346-438. See specification at page 6, lines 5-23. This is a description of what the BLNK protein is not just what it does and as such meets an adequate written description requirement.

The Examiner cites to *Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd*, 18 USPQ2d, 1016 which states:

> Conception of chemical compound requires that inventor be able to define compound so as to distinguish it from other materials, and to describe how to obtain it, rather than simply defining it soley by its principal biological property.

Applicant's define a BLNK protein, which includes three distinct structural regions so that one of ordinary skill in the art would be able to distinguish it from other materials and be able to obtain a BLNK protein without undue experimentation.

The Examiner further states that no guidance is provided for determining which nucleotide positions may be changed for determining the specific sequences that are within the scope of the claims. One of ordinary skill in the art would be able to screen for various mutants that retained the same structural integrity of a BLNK protein and maintained the same biological properties so desired, such as binding to Grb2. Accordingly, one of ordinary skill in the art would be able to determine the specific sequences that are within the scope of the claims.

Claim 43 is directed to an antibody, which will bind to the BLNK protein according to any one of Claims 35 to 41. Support for claim 43 is found in the specification at page 15, lines 6-18. One of ordinary skill in the art would be able to screen for antibodies, which bind to BLNK without undue experimentation. The specification adequately conveys to one of ordinary skill in the art that the applicants had possession of the claimed invention at the time the application was filed. Therefore 35 U.S.C. 112, first paragraph: written description has been met. Applicants respectfully request the withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, second paragraph: Indefiniteness

Claims 37, 41, 43-45 are rejected to as lacking a positive real time definition because the phrase "will bind", these claims have all been amended for clarity by deleting the term "will binds" and changing it to "binds". In addition claim 45 has been amended for clarity. Accordingly, Applicants respectfully request the withdrawal of the rejections.

Rejection under Double patenting obviousness-type rejection

Claims 35-37 and 39-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,994,522. Applicants respectfully request that this rejection be held in abeyance until there is an indication of allowable subject matter.

Applicants submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 781-1989.

Respectfully submitted,

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